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(54) PHARMACEUTICAL DOSAGE FORMS

(71) We, JOHN WYETH & BROTHER LIMITED, a British Company of Huntercombe Lane South, Taplow, Maidenhead, Berkshire SL6 0PH, do hereby declare the invention for which we pray that a patent may be granted to us and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to pharmaceutical dosage forms, to a method of preparing such dosage forms, and to packages containing the dosage forms.

Many pharmaceuticals are administered orally in the form of solid shaped articles such as tablets, pills and capsules. Generally the tablet, pill or capsule has to be swallowed from the mouth to the stomach to enable the pharmaceutical to be absorbed in the gastro-enteric system. However, in some cases there is the problem that swallowing is difficult or not feasible. Some subjects, particularly paediatric and geriatric patients, may be unco-operative and spit the tablet out instead of swallowing it. A similar difficulty can be present in administering pharmaceuticals to non-human animals in veterinary treatment in that animals may also be unco-operative about taking tablets. The invention, in one aspect, seeks to avoid this problem by providing a pharmaceutical dosage form that disintegrates rapidly in the mouth. Some embodiments of the invention dissolve so rapidly in the saliva of the mouth, for instance, in one or two seconds, that there is hardly time for an unco-operative subject to spit the product out.

Accordingly the present invention provides a solid pharmaceutical dosage form for oral administration, which comprises a network of a pharmaceutically acceptable water-soluble or water-dispersible carrier material carrying a unit dosage of pharmaceutical substance, the carrier material being inert towards the pharmaceutical substance, the network having been obtained by subliming solvent from a composition in the solid state,

the composition comprising the pharmaceutical substance and a solution of the carrier material in a solvent, such that the solid dosage form is capable of being rapidly disintegrated by water (as hereinafter defined).

By "rapidly disintegrated" is meant that the dosage forms are disintegrated in water within 10 seconds when tested by the following procedure which is analogous to the Disintegration Test for Tablets, B.P. 1973:—

Apparatus

A glass or suitable plastic tube 80 to 100 mm long, with an internal diameter of about 28 mm and an external diameter of 30 to 31 mm. and fitted at the lower end, so as to form a basket, with a disc of rustproof wire gauze complying with the requirements for a No. 1.70 sieve (B.P. 1973 page A136).

A glass cylinder with a flat base and an internal diameter of about 45 mm containing water not less than 15 cm deep at a temperature between 36° and 38°C.

The basket is suspended centrally in the cylinder in such a way that it can be raised and lowered repeatedly in a uniform manner so that at the highest position the gauze just breaks the surface of the water and at the lowest position the upper rim of the basket just remains clear of the water.

Method

Place one shaped article in the basket and raise and lower it in such a manner that the complete up and down movement is repeated at a rate equivalent to thirty times a minute. The shaped articles are disintegrated when no particle remains above the gauze which would not readily pass through it. No such particle should remain after 10 seconds.

Preferably the dosage forms disintegrate (dissolve or disperse) within 5 seconds or less.

The network of water-soluble or water-dispersible carrier has interstices dispersed throughout when it has been obtained in the manner indicated above. The network of

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carrier material is of generally low density. For example the density may be within the range 10 to 200 mg/cc e.g. 10 to 100 mg/cc, preferably 30 to 60 mg/cc. The density of the dosage form may be effected by the amount of pharmaceutical substance, or any other ingredients, incorporated into the article and may be outside the above mentioned preferred limits for the density of the network. The network which is similar in structure to a solid foam enables a liquid to enter the product through the interstices and permeate through the interior. Permeation by aqueous media exposes the carrier material of both the interior and exterior of the product to the action of the aqueous media whereby the network of carrier material is rapidly disintegrated. The network structure is of a porous nature and enhances disintegration of the product as compared with ordinary solid shaped pharmaceutical dosage forms such as tablets, pills, capsules, suppositories and pessaries. Rapid disintegration results in rapid release of the pharmaceutical substance carried by the matrix.

The carrier material used in the product of the invention may be any water-soluble or water-dispersible material that is pharmacologically acceptable and inert to the pharmaceutical substance and which is capable of forming a rapidly disintegratable network. We prefer to use water-soluble material as the carrier since this results in the most rapid disintegration of the network when the product is placed in an aqueous medium. We have found that a particularly advantageous carrier may be formed from polypeptides such as gelatin, particularly gelatin which is partially hydrolysed, e.g. by heating in water. For example, the gelatin may be partially hydrolysed by heating a solution of the gelatin in water, e.g. in an autoclave at about 120°C. for up to 2 hours, e.g. from about 5 minutes to about 1 hour, preferably from about 30 minutes to about 1 hour. The hydrolysed gelatin is preferably used at concentrations of about 1 to 6% weight/vol., most preferably at 2 to 4% e.g. about 3%. Other carrier materials may be used in place of partially hydrolysed gelatin for example polysaccharides such as hydrolysed dextran, dextrin and alginates (e.g. sodium alginate) or mixtures of above mentioned carriers with each other or with other carrier materials such as polyvinyl alcohol, polyvinylpyrrolidone or acacia.

The pharmaceutical dosage form of the invention may be employed to administer a wide variety of pharmaceutical substances. In this specification the term "pharmaceutical substances" not only includes medicaments for administration to human and non-human animals but also contraceptives (particularly oral contraceptives). Typical drugs which can be administered by means of this inven-

tion include, for example, drugs for treating coronary disorders, e.g. digoxin; oral vaccines; enzymes; anti-anginal drugs, e.g. glyceryl trinitrate; peripheral vasodilators and anti-hypertensives e.g. indoramin; vasoconstrictors, e.g. ergotamine; analgesics e.g. meptazinol, pentazocine; hypnotics; major and minor tranquilizers e.g. lorazepam, oxazepam, temazepam; anti-depressants e.g. citalopram; anticonvulsants e.g. clonazepam; CNS stimulants e.g. pemoline; muscle relaxants e.g. orphenadrine; neuro-muscular drugs e.g. pyridostigmine; gonadal hormones and oral contraceptives e.g. ethynyl oestradiol, norgestrel; corticosteroids e.g. prednisolone; local anaesthetics; anti-inflammatories e.g. oxaprozin; drugs acting on the uterus e.g. hyoscine butyl bromide; spermicides e.g. nonoxonyl - 9; anti-allergics e.g. triprolidine and drugs relieving poisoning and metabolic dysfunction e.g. methysergide. The pharmaceutical dosage form can be used, for example, for administration of drugs which are normally absorbed via the gastro intestinal tract and it is also useful for administration of drugs (e.g. nitroglycerin) via the buccal route since such drugs may be very rapidly absorbed by the use of the present invention.

The dosage forms of the present invention may incorporate ingredients in addition to the chemical or pharmaceutical substance. For example the pharmaceutical dosage form of the present invention may incorporate pharmaceutically acceptable adjuvants. Such adjuvants include, for example, colouring agents, flavouring agents, preservatives (e.g. bacteriostatic agents), and the like.

The present invention also provides a process for preparing the pharmaceutical dosage forms. Thus there is provided a process for preparing a solid pharmaceutical dosage form for oral administration, which process comprises subliming solvent from a composition comprising a pharmaceutical substance and a solution in a solvent of a pharmacologically acceptable water-soluble or water-dispersible carrier material inert towards the pharmaceutical substance, the composition being in the solid state in a mould, so as to produce a network of carrier material carrying a unit dosage of the pharmaceutical substance such that the dosage form is capable of being rapidly disintegrated by water (as hereinbefore defined).

The sublimation is preferably carried out by freeze drying a composition comprising the pharmaceutical substance and a solution of the carrier material in a solvent. The composition may include additional ingredients, such as those mentioned above. The solvent is preferably water but it may contain a co-solvent (such as an alcohol e.g. tert-butyl alcohol) to improve the solubility of the pharmaceutical substance. The composition

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may also contain a surfactant e.g. Tween 80 [polyoxyethylene (20) sorbitan mono-oleate; Tween is a Registered Trade Mark]. The surfactant may help to prevent the freeze dried product sticking to the surface of the mould. It may also aid in the dispersion of the pharmaceutical substance.

The mould may comprise a number of cylindrical or other shape depressions, each of a size corresponding to the desired size of the shaped article.

In one embodiment the mould comprises a metal plate (e.g. an aluminium plate) containing one or more depressions. In a preferred process using such a mould, the mould is cooled with a cooling medium (e.g. liquid nitrogen or solid carbon dioxide). When the mould is cooled a predetermined amount of water containing the carrier material, the pharmaceutical substance and any other desired ingredient is fed into the depression(s). When the contents of the depression(s) are frozen the mould is subjected to reduced pressure, and, if desired, controlled application of heat to aid the sublimation) in a freeze dryer. The pressure can be below about 4 mm.Hg; we prefer to employ pressures of below 0.3 mm Hg, for example 0.1 to 0.2 mm. The freeze dried products may then be removed from the depressions in the mould and stored for future use, e.g. in airtight jars or other suitable storage containers.

The dosage forms are rather fragile and it is an advantage to restrict handling of them to a minimum. Therefore, a preferred aspect of the invention avoids transferring the dosage form from a mould to a suitable storage container by employing, as the mould, depressions in a sheet of filmic material and then adhering a covering sheet around the depressions to enclose the shaped articles. Accordingly the present invention, in a preferred aspect, provides a process for preparing packages containing one or more solid pharmaceutical dosage forms, which process comprises subliming solvent from a composition comprising a pharmaceutical substance and a solution in a solvent of a pharmaceutically acceptable water-soluble or water-dispersible carrier material inert towards the pharmaceutical substance, the composition being in the solid state in one or more depressions in a sheet of filmic material, so as to produce in the depression or depressions a network of carrier material carrying a unit dosage of the pharmaceutical substance such that the resulting dosage form is capable of being rapidly disintegrated by water (as hereinbefore defined), and then adhering a covering sheet around the depression or depressions to enclose the dosage form. This process of the invention enables packages of the shaped articles to be produced in which handling of the individual shaped articles may be

eliminated until the user, e.g. the patient, removes the product from the depression in the package immediately prior to use.

The sublimation is preferably carried out by freeze drying a composition comprising the pharmaceutical substance and a solution of the carrier material in a solvent, e.g. water.

The invention also provides a package comprising a sheet of filmic material having one or more depressions therein, one or more of the depressions containing a dosage form (according to the present invention), and a covering sheet adhering to the sheet of filmic material so as to enclose the dosage form or forms.

By a sheet of filmic material is meant a sheet of material that, although thin, is sufficiently stiff to be formed with one or more depressions. The filmic material and the covering sheet may, for example, be similar to those employed in conventional blister packs used for packaging tablets and like medicament forms. For example, the filmic material is usually a suitable stiff but resilient film and it is normally stronger than the covering layer. Preferably the filmic material is made of thermoplastic material so that the depressions may be formed by, for example, thermoforming. The filmic material may, for example, be a polyvinyl chloride film or a laminate such as polyvinylchloride/polyvinylidenechloride, polyvinylchloride/polytetrafluoroethylene or polyvinylchloride/polyvinylidenechloride/polyethylene.

The dosage forms are moisture sensitive and therefore it may be advisable to use a thermoplastic material which is particularly moisture resistant or to use a non-thermoplastic moisture-resistant filmic material, for example a stiff aluminium foil in which the depressions can be formed by cold pressure forming. Alternatively, if the dosage forms are particularly moisture-sensitive the complete package may be enclosed in a removable moisture-resistant outer case, e.g. an aluminium foil bag.

The covering sheet is preferably an aluminium foil or aluminium foil laminate (e.g. aluminium foil/paper) which may be adhered to the filmic material around the depressions by, for example, a heat sensitive adhesive material. The dosage forms are rather fragile and it is not generally possible to remove them from the package by forcing them through the covering sheet, as with conventional blister packs, unless the covering sheet is relatively thin. Accordingly, the covering sheet is preferably adhered to the filmic material such that it may be peeled away from the filmic material by the user to expose the dosage forms in their depressions. Preferably the covering sheet around one or more of the depressions is inherently weakened by, for example, surface perforations so that the covering sheet may be removed in stages to

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expose the dosage forms in succession. The user may thus remove the individual dosage forms from the package as desired. The covering sheet may be made of a material other than aluminium foil or aluminium foil laminate (such as a plastic film), if it adheres by peelable means to the filmic material. The composition may be freeze dried in the depressions of the filmic material by, for example, procedures analogous to those described above. For example, a measured quantity of the composition may be added to each depression and the filmic material containing the filled depressions then cooled with a cooling medium e.g. liquid nitrogen or preferably solid carbon dioxide. When the contents of the depressions are frozen the filmic material and contents may be subjected to reduced pressure and, if desired, controlled application of heat to aid the sublimation. A large sheet of filmic material (equivalent in size to many of the desired finished packages) containing numerous depressions may be subjected to the freeze drying procedure and the covering sheet may then be adhered to it. The filmic material with the adhering covering sheet may then be cut into the desired number of finished packages each having, for example, about 6 to 25 depressions, each depression containing a shaped article.

The following examples illustrate the invention:

EXAMPLE 1

(a) Preparation of hydrolysed gelatin solution

Gelatin B.P.	30.00 g.
Purified water to	1000.00 ml.

The gelatin is dissolved in the water with the aid of heat and constant stirring. The resulting solution is autoclaved at 121°C (15 p.s.i.) for one hour. The solution is allowed to cool to room temperature.

(b) Preparation of pharmaceutical dosage form

Lorazepam	1.00 g.
Colour (F.D.C. Yellow No. 5)	0.25 g.
Orange flavour (Norda spray dried)	0.5 g.
Gelatin solution to	1000.00 ml.

An aluminium mould containing 75 cylindrical depressions (each depression being about 0.5 cm diameter and 1 cm deep) is cooled to about -192°C in liquid nitrogen and contained in a stainless steel tray. The lorazepam, colour and flavour are mixed with the gelatin solution and mixing continued while 1 ml. of the mixture is injected by hypodermic syringe into each depression. When the contents of each depression are

frozen the mould is placed into a vacuum chamber at room temperature and a vacuum of 0.3 mm Hg. is applied overnight. The freeze dried pharmaceutical dosage forms, each containing 0.5 mg. of lorazepam, are then removed from the depressions and stored in airtight jars.

The pharmaceutical dosage forms disintegrate rapidly, for example, in two seconds or less, when taken orally.

EXAMPLE 2

The method of Example 1(b) is repeated substituting 2.00 g. nitroglycerin for the 1.00 g. lorazepam and using appropriate pharmaceutically acceptable colours and flavours to give pharmaceutical dosage forms each containing 1.00 mg. of nitroglycerin.

EXAMPLE 3

The method of Example 1(b) is repeated substituting 2.00 g. digoxin for the 1.00 g. lorazepam and using appropriate pharmaceutically acceptable colours and flavours to give pharmaceutical dosage forms each containing 1.00 mg. of digoxin.

EXAMPLE 4

The method of Example 1(b) is repeated substituting 2.00 g. ergotamine for the 1.00 g. lorazepam and using appropriate pharmaceutically acceptable colours and flavours to give pharmaceutical dosage forms each containing 1.00 mg. of ergotamine.

EXAMPLE 5

Lorazepam	5 g.	
Tween 80 [polyoxyethylene (20) sorbitan monoleate]	0.5 g.	
Sucrose	30 g.	
Gelatin solution [from Example 1(a)]	to 1000 ml.	

A p.v.c. sheet of approximate size 220×330 mm containing 150 cylindrical depressions (each depression being about 1.4 cm. diameter and 0.7 cm. deep) is cooled with solid carbon dioxide. The lorazepam, Tween 80 and Sucrose (flavour) are mixed with the gelatin solution and mixing continued while 0.5 ml of the solution is placed in each of the depressions. When the contents of the depressions are frozen the pvc sheet is immediately placed in a vacuum chamber and a vacuum of about 0.1 mm Hg. is applied for 8 hours. The sheet containing the freeze dried pharmaceutical dosage forms is then removed from the vacuum chamber and an aluminium foil is sealed to the sheet surrounding the depressions by means of a heat sensitive adhesive. The surface of the metal foil is then surface-perforated around each depression. The pvc sheet with its adhering metal foil is then cut into 25 packs, each pack having 6 depressions. Each

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	depression contains a pharmaceutical dosage form containing 2.5 mg. of lorazepam. The dosage forms disintegrate rapidly, in 1 to 5 seconds, when taken orally.		60
5	EXAMPLE 6		
	Meptazinol 80 g.		
	Sucrose 40 g.		
	Gelatin solution [from Example 1(a)] to 1000 ml.		
10	The procedure of Example 5 is repeated using the above composition to give packages containing pharmaceutical dosage forms each containing 40 mg. of meptazinol.		
	EXAMPLE 7		
15	Oxaprozin 200 g.		
	Sucrose 40 g.		
	3% Hydrolyzed Gelatine Solution to 1000 ml.		
20	The hydrolysed gelatine solution is prepared as in Example 1(a) above. The procedure of Example 5 above is repeated, the oxaprozin being dispersed in the gelatine solution with the aid of ultrasonic vibrations. The packages produced by the procedure contain pharmaceutical dosage forms each containing 200 mg. of oxaprozin.		
	EXAMPLE 8		
	Lorazepam 3.33 g.		
	Sodium alginate 15 g.		
30	Dextran (M.wt. approx 40,000) 35 g.		
	Dextrose 17.5 g.		
	Distilled water to 1000 ml		
35	A pvc sheet of approximate size 220×330 mm. containing 150 cylindrical depressions (each depression being about 1.4 cm. diameter and 0.7 cm. deep) is cooled with solid carbon dioxide.		
40	3.33 g. of lorazepam is suspended in the water containing 15 g. sodium alginate, 35 g. dextran and 17.5 g. dextrose with the aid of ultrasonic vibrations. 0.75 ml. of the suspension is introduced into each depression. The contents of the depressions are freeze dried and packs prepared each containing six pharmaceutical dosage forms by the procedure described in Example 5. Each pharmaceutical dosage form contains 2.5 mg. of lorazepam.		
50	EXAMPLE 9		
	Lorazepam 3.33 g.		
	Dextrin 50 g.		
	Polyvinylpyrrolidone 30 g.		
	Tween 80 0.2 g.		
55	Distilled water to 1000 ml.		
	A pvc sheet similar to that in Example 5 is cooled with solid carbon dioxide. A mixture of the above composition is prepared		
	by a procedure analogous to that of Example 8 and 0.75 ml of the mixture introduced into each depression in the pvc sheet. The contents of the depressions are freeze dried and packs prepared each containing six pharmaceutical dosage forms by the procedure described in Example 5. Each pharmaceutical dosage form contains 2.5 mg. of lorazepam.		65
	EXAMPLE 10		
	Lorazepam 3.33 g.		
	Polyvinylalcohol (M.Wt. approx 1400) 20 g.		
	Polyvinylpyrrolidone 20 g.		
	Sucrose 30 g.		
	Tween 80 0.2 g.		
	Distilled water to 1000 ml.		
	A pvc sheet similar to that in Example 5 is cooled with solid carbon dioxide. 20 G. of polyvinylalcohol is dissolved in about 500 ml. of hot distilled water and the solution then cooled. 20 G. of polyvinylpyrrolidone, 30 g. of sucrose and 0.2 g. Tween 80 are added and the mixture shaken until all the solids are dissolved. 3.33 g. of lorazepam is added and dispersed with the aid of ultrasonic vibrations. The final volume of solution is adjusted to 1000 ml. with distilled water.		70
	0.75 ml of the solution is added to each depression in the pvc sheet the contents of the depressions are freeze dried and packs prepared each containing six pharmaceutical dosage forms by the procedure described in Example 5. Each pharmaceutical dosage form contains 2.5 mg. of lorazepam.		75
	EXAMPLE 11		
	Lorazepam 3.33 g.		
	Acacia 20 g.		
	Sucrose 30 g.		
	Polyvinylpyrrolidone 30 g.		
	Tween 80 0.2 g.		
	Distilled water to 1000 ml.		
	A pvc sheet similar to that in Example 5 is cooled with solid carbon dioxide. 20 g. of Acacia is placed in a dry 1000 ml. volumetric flask. About 10 ml. of absolute alcohol is added and the flask shaken to wet the acacia powder. 500 ml. of distilled water is introduced and shaken to yield a homogeneous solution. 30 g. Sucrose, 30 g. polyvinylpyrrolidone, 0.2 g. Tween 80 and 3.33 g. lorazepam are dispersed into the solution with the aid of ultrasonic vibrations. The final volume is adjusted to 1000 ml. with distilled water. 0.75 ml. of the composition is added to each depression in the pvc sheet. The contents of the depressions are freeze dried and packs prepared each containing six pharmaceutical dosage forms by the procedure described in Example 5. Each pharmaceutical dosage form contains 2.5 mg. of lorazepam.		80
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WHAT WE CLAIM IS:—

1. A solid pharmaceutical dosage form for oral administration, which comprises a network of a pharmaceutically acceptable water-soluble or water-dispersible carrier material carrying a unit dosage of pharmaceutical substance, the carrier material being inert towards the pharmaceutical substance, the network having been obtained by subliming solvent from a composition in the solid state, the composition comprising the pharmaceutical substance and a solution of the carrier material in a solvent, such that the solid dosage form is capable of being rapidly disintegrated by water (as hereinbefore defined).
2. A pharmaceutical dosage form as claimed in Claim 1 wherein the carrier material is partially hydrolysed gelatin.
3. A pharmaceutical dosage form as claimed in Claim 1 wherein the carrier material is dextrin.
4. A pharmaceutical dosage form as claimed in Claim 1 wherein the carrier material is hydrolysed dextran or an alginate.
5. A pharmaceutical dosage form as claimed in Claim 1 wherein the carrier material is a mixture of one or more of the carrier materials specified in any one of the Claims 2 to 4 with polyvinyl alcohol, polyvinylpyrrolidone or acacia.
6. A pharmaceutical dosage form substantially as hereinbefore described with reference to any one of Examples 1 to 4.
7. A pharmaceutical dosage form substantially as hereinbefore described with reference to any one of Examples 5 to 11.
8. A process for preparing a solid pharmaceutical dosage form for oral administration, which process comprises subliming solvent from a composition comprising a pharmaceutical substance and a solution in a solvent of a pharmacologically acceptable water-soluble or water-dispersible carrier material inert towards the pharmaceutical substance, the composition being in the solid state in a mould so as to produce a network of carrier material carrying a unit dosage of the pharmaceutical substance such that the dosage form is capable of being rapidly disintegrated by water (as hereinbefore defined).
9. A process as claimed in Claim 8 wherein the composition contains a colouring agent, a flavouring agent or a preservative.
10. A process as claimed in Claim 8 or 9 in which the solvent is water.
11. A process as claimed in Claim 10 wherein the water contains a co-solvent and/or a surfactant.
12. A process as claimed in any one of Claims 8 to 10 wherein the carrier material is partially hydrolysed gelatin.
13. A process as claimed in any one of Claims 8 to 10 wherein the carrier material is dextrin.
14. A process as claimed in any one of Claims 8 to 10 wherein the carrier material is hydrolysed dextran or an alginate.
15. A process as claimed in any one of Claims 8 to 11 wherein the carrier material is a mixture of one or more of the carrier materials specified in any one of Claims 12 to 14 with polyvinyl alcohol, polyvinylpyrrolidone or acacia.
16. A process as claimed in any one of claims 8 to 10, 12 and 13 wherein the mould is a depression in a metal plate.
17. A process as claimed in any one of claims 8 to 15 wherein the mould is a depression in a sheet of filmic material.
18. A process as claimed in claim 17 wherein the filmic material is thermoplastic material.
19. A process for preparing a pharmaceutical dosage form substantially as hereinbefore described with reference to any one of Examples 1 to 4.
20. A process for preparing a pharmaceutical dosage form substantially as hereinbefore described with reference to any one of Examples 5 to 11.
21. A pharmaceutical dosage form whenever made by a process claimed in any one of claims 8 to 10, 12, 13, 16 and 19.
22. A pharmaceutical dosage form whenever made by a process as claimed in any one of claims 11, 14, 15, 17, 18 and 20.
23. A process for preparing packages containing one or solid pharmaceutical dosage forms, which process comprises subliming solvent from a composition comprising a pharmaceutical substance and a solution in a solvent of a pharmacologically acceptable water-soluble or water-dispersible carrier material inert towards the pharmaceutical substance, the composition being in the solid state in one or more depressions in a sheet of filmic material, so as to produce in the depression or depressions a network of carrier material carrying a unit dosage of the pharmaceutical substance such that the resulting dosage form is capable of being rapidly disintegrated by water (as hereinbefore defined), and then adhering a covering sheet around the depression or depressions to enclose the dosage form.
24. A process as claimed in Claim 23 wherein the solvent is water.
25. A process as claimed in Claim 23 or 24 wherein the carrier material comprises partially hydrolysed gelatin.
26. A process as claimed in Claim 23 or 24 wherein the carrier material comprises dextrin, hydrolysed dextran or an alginate.
27. A process as claimed in any one of claims 24 to 26 wherein the filmic material is thermoplastic material.
28. A process as claimed in any one of claims 24 to 27 wherein the filmic material is a polyvinylchloride film or a polyvinylchloride/polyvinylidenechloride, polyvinyl-

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	chloride/polytetrafluoroethylene or polyvinylchloride/polyvinylidenechloride/polyethylene laminate.	
5	29. A process as claimed in any one of claims 24 to 28 wherein the covering sheet is an aluminium foil or aluminium foil laminate.	20
10	30. A process for preparing packages containing pharmaceutical dosage forms substantially as hereinbefore described with reference to any one of Examples 5 to 11.	
	31. A package whenever prepared by a process claimed in any one of claims 23 to 30.	
15	32. A package comprising a sheet of filmic material having one or more depressions	25
	therein, one or more of the depressions containing a pharmaceutical dosage form as claimed in any one of claims 1 to 8, 21 and 22 and a covering sheet adhering to the sheet of filmic material so as to enclose the pharmaceutical dosage form or forms.	
	33. A package as claimed in claim 32 wherein the filmic material is as specified in claim 28.	
	34. A package as claimed in claim 32 or 33 wherein the covering sheet is as specified in claim 29.	
	K. J. S. BROWN, Chartered Patent Agent.	

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